UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,781	05/09/2007	Sungho Jin	15977-34	7355

28221 7590 12/30/2009

PATENT DOCKET ADMINISTRATOR
LOWENSTEIN SANDLER PC
65 LIVINGSTON AVENUE
ROSELAND, NJ 07068

EXAMINER	
REDDIG, PETER J	
ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
12/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,781	JIN ET AL.	
	Examiner	Art Unit	
	PETER J. REDDIG	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *18-20 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17, 21, 22, 24, and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed September 8, 2009, in response to the Office Action of June 5, 2009 is acknowledged and has been entered. Previously pending claims 26-28 have been cancelled, claims 1-3, 7, 8, 10-13, 15, and 21-25 have been amended. Claims 1-25 are pending. Claims 18-20, 23 were previously withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claims 1-17, 21, 22, 24, and 25 are currently under consideration.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is drawn to the method of claim 1, wherein the particles further comprise medication, wherein the medication is delivered to the target cell upon and the application of the magnetic field. It is indefinite "upon" what or when the medication is delivered to the target cell.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 1, 2, 5, 6, 8, 9, 15, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/17611 A1 (Fredriksson et al. March 13, 2001).

WO 01/17611 A1 teaches using magnetic nano-particles to damage and destroy cell structures with alternating magnetic field by shear forces. WO 01/17611 A1 teaches coating the particles with an antibody, a bio-compatible material. WO 01/17611 A1 teaches using two magnetic fields and inducing heat hysteresis and structural damage to the cells. See p. 2-5. Figs. 1-3, and claims 1-10. WO 01/17611 A1 teaches that the direction of the magnetic field is alternated, which will alternate the directions of the particles, i.e. it will oscillate. See p. 4. Given that the nanoparticles claimed encompass spherical particles which have no predefined orientation, lateral oscillation encompasses any oscillation.

4. Claims 1-8, 12, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Halbreich et al. (J. Magnetism and Magnetic Materials June 5, 2002 248:276-285).

Halbreich et al. teach that ferromagnetic particles rotate when placed in an alternating magnetic field. See p. 277-left col. Halbreich et al. teach injecting mice with arabinogalactan, a bio-compatible polymer, coated ferrofluid (HS-USPIO) that binds the arabinogalactan receptor on hepatocytes and is endocytosed by the cells. See p. 277-right col. and p 278 and Josephson et al. (Magnetic Resonance Imaging 1990 8:637-646, Abstract and Materials and Methods, in particular) cited as ref 9 by Halbreich. Halbreich et al. teach that application of a 1000 kHz

alternating magnetic field induced magnetocytoloysis in mouse hepatocytes. See abstract, p. 278-right col., Table 1, and 284. Halbreich et al. also teach magnetic nano-particles bound to tamoxifen or estrogen that were delivered to cells and the cells were damage upon application of a magnetic field. See p. 277-left col.

Although the reference does not specifically state that the magnetic field laterally oscillates the nanoparticles to structurally damage the target cell, the claimed method appears to be the same as the prior art method, absent a showing of unobvious differences, i.e. providing particles comprising one or more nanoparticles of magnetic material, contacting the particles with the target cell and applying a magnetic field to the particles to induce motion of the particles, whereby the motion of the particles in contact with the target cell inflicts structural damage to the target cell. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the method of the prior art does not possess the same material, structural and functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed method is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA).

5. Claims 1, 2, 5-9, 12, 13, 15, and 24 are rejected under 35 U.S.C. 102(a) and 35 U.S.C. 102(e) as being anticipated by USPN 6,514,481 (Prasad et al. published 2/4/2003, effective filing date 11/22/1999).

USPN 6,514,481 teaches the lysis of a targeted cell with magnetic nanoparticles coated with biocompatible targeting peptides/ LHRH and a silica (silicon dioxide, See Dorland's Medical Dictionary for Healthcare Consumers (silica 2007)) shell by application of a magnetic

field that moves the particles out of the cells. See claims 1-21, Example 4, and Fig. 6. USPN 6,514,481 teaches injection of nanoparticles into tissue for tumor treatment. See col. 1-lines 35-50. USPN 6,514,481 teaches that the LHRH magnetic particles are taken up by endocytosis. See col. 7-lines 20-25 and Examples 3. USPN 6,514,481 teaches that the particles are elongated along one dimension. See Fig. 2. . USPN 6,514,481 teaches confirming the contact of the particles to the target cells prior to apply the magnetic field. See Examples 3 and 4.

Although the reference does not specifically state that the magnetic field rotates or laterally oscillates the nanoparticles to structurally damage the target cell, the claimed method appears to be the same as the prior art method, absent a showing of unobvious differences, i.e. providing particles comprising one or more nanoparticles of magnetic material, contacting the particles with the target cell and applying a magnetic field to the particles to induce motion of the particles, whereby the motion of the particles in contact with the target cell inflicts structural damage to the target cell. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the method of the prior art does not possess the same material, structural and functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed method is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

> having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6.. Claims 3, 4, 7, 10, 11, 16, 17, 22, 24, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/17611 A1 (Fredriksson et al. March 13, 2001) as applied to claims 1, 2, 5, 6, 8, 9, 15, and 21 above, in view of Chung et al. (J. Controlled Release 2000 65: 93-103, previously cited), in view of Jordan et al. (J. Magnetism and Magnetic Materials, 2001 225:118-126, IDS), in view of Shinkai et al. (Jpn. J. Cancer Res. 92:1138-1146, previously cited), in view of Alexiou et al. (Cancer Research Dec. 2000, 60: 6641-6648, previously cited), and in view of Alexiou et al. (J. Drug Targeting, April 2003, 11: 139-149, previously cited).

WO 01/17611 A1 teach as set forth above, but does not teach magnetic navigation, magnetic transfection, injection of the particles, particles that comprise a heat sensitive reservoir of medication, that the application of the magnetic field to the nanoparticles provides heat to effect delivery of the medication, or a magnetic field that is an AC magnetic field at a frequency in range of 1KHz to 5 MHz. WO 01/17611 A1 do not teach confirming the adjacency of the particles to diseased cells or tissue prior to applying the magnetic field by MRI imaging. WO 01/17611 A1 teaches using an alternating magnetic field up to 30 MHz.

Chung et al. teach thermo-sensitive polymeric micelles comprised of AB block copolymers of PIPAAm with either poly(butly methacrylate or polystyrene for the thermo-responsive drug delivery of adriamycin to cells, see Abstract, Fig. 4 and 5 and table 1. Chung et al. teach that the thermo-responsiveness of the micelles can increase the targeting efficiency via a stimuli-responsive targeting process that utilizes local heating at solid tumor sites. Chung et al. teach that the thermo-response is expected to exhibit multiple targeting functions: a passive and a stimuli-responsive targeting mechanism, plus the therapeutic effect of hyperthermia by local heating, see p. 94 1st col. Chung et al. teach that hyperthermia enhances the cytotoxicity of some anticancer drugs by synergistic effects, see p. 94- 2nd col. Chung et al. teach that thermo-sensitive lipsosomes have been used to achieve targeted drug delivery, see p. 94- 2nd col.

Jordan et al. teach that hyperthermia intensifies the efficacy of radiation and/or chemotherapy, see pp.118-119, Introduction and state of the art. Jordan et al. teach that ferromagnetic seeds can be used to induce localized hyperthermia with AC magnetic field of 25-50 kHz, see p. 119-2nd col. Jordan et al. teach using magnetic nanoparticles to induce

hyperthermia in tumors with a device using a 100 kHz AC magnetic field, see section 3, pp. 120-124 and Fig. 2-3.

Shinkai et al. teach that hyperthermia is a therapy based on the fact that tumor cells are more sensitive to temperature in the range of 42-45˚C than normal tissues, see p. 1138. Shinkai et al. teach using antibody targeted magnetoliposomes to induce hyperthermia with a 118 kHz AC magnetic field to treat renal cell carcinomas in mice, see Abstract, Materials and Methods, Figs. 4-7 and Tables 1-2.

Alexiou et al. (2000) teach using magnetic nanoparticles surrounded by starch polymers bound to mitoxantrone (MTX) a chemotherapeutic agents that inhibits DNA and RNA synthesis to treat squamous cell carcinoma by magnetically targeting the MTX- magnetic nanoparticles to the tumors, see Abstract, Materials and Methods, and Figures. Alexiou et al. (2000) teach administering the nanoparticles by intravenous intra-arterial infusion, see Table 2. Alexiou et al. (2000) teach that the magnetic particles can be modified with monoclonal antibodies, lectins, peptides, hormones, or genes to make delivery of the compounds more efficient and highly specific, see p. 6648-1st col. Alexiou et al. teach localizing the magnetic particles with MRI after application of the magnetic field, see Fig. 16.

Alexiou et al. (2003) teach that magnetic drug targeting leads to uptake of the particles by cells, see Figure 3 and 4. Thus, the method of Alexiou et al (2000) is a method of magnetic transfection.

It would have been *prima facie* obvious at the time the invention was made and one of skill in the art would have be motivated to combine the teachings of WO 01/17611 and Chung et al. and coat the nanoparticles with the thermo-sensitive co-polymers bound to the medicine of

Chung et al. to provide greater control of the timing of the release of the drug upon providing an appropriate increase in temperature by magnetic field induced hyperthermia. Furthermore, one would have been motivated to use a heat induced drug release because Jordan et al. and Chung et al. teach hyperthermia intensifies the efficacy of radiation and/or chemotherapy and Shinkai et al. teach that hyperthermia induced in magnetic particle is effective for cancer treatment. Additionally, it would have been *prima facie* obvious at the time the invention was made and one of skill in the art would have be motivated to use an AC magnetic field in the frequency range of 1 KHz-5MHz because Jordan et al. and Shinkai et al. teach that AC magnetic fields in this range are routinely used in the art for the induction of magnetic hyperthermia.

It would have been *prima facie* obvious at the time the invention was made and one of skill in the art would have be motivated to combine the teachings of WO 01/17611 and Alexiou et al. (2000) and Alexiou et al. (2003) and magnetically direct the nanoparticles to the cell and magnetically transfect the particles after injection into a test animal because Alexiou et al. (2000) teach that magnetic drug targeting offers a unique opportunity to treat malignant tumors loco-regionally without systemic toxicity. See Abstract. Furthermore, it would have been *prima facie* obvious at the time the invention was made and one of skill in the art would have be motivated to confirm the adjacency of the magnetic nano-particles loaded with medication in a thermo-sensitive reservoir to the tumors using MRI to ensure the proper localization of the magnetic particles to the disease tumor tissue before thermally inducing the release of the drug with a AC magnetic field to prevent non-specific release of the drugs in normal tissues if the nano-particles have not been properly localized. Thus, given the above, one of skill in the art would have been motivated with a reasonable expectation of success to make and used the claimed method.

7. Claims 3, 7, 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/17611 A1 (Fredriksson et al. March 13, 2001) as applied to claims 1, 2, 5, 6, 8, 9, 15, and 21 above, in view of USPN 6,231,496 (Wilk et al. May 15, 2001).

WO 01/17611 A1 teaches as set forth above and using an alternating magnetic field up to 30 MhZ. WO 01/17611 A1 does not teach delivery of medication, injection of the particles, magnetic nanoparticles elongated long one dimension and rotating the elongated particles at a frequency in the range of 1 Hz to 500 Hz.

USPN 6,231,496 teach using magnetized metal particles that are advantageously tapered to form a sharp end for sterilization and cancer treatment by injecting the particles and orienting the particles with a magnet and pulling them into the tissue with a magnet. See cols. 1 and 2 and claims 1-21. USPN 6,231,496 teaches coating the particles with an irritant for treatment and antibiotics and anti-growth factor. See col. 7-lines 1-5 and claims 1-21

It would have been *prima facie* obvious at the time the invention was made and one of skill in the art would have be motivated to combine the teachings of WO 01/17611 and USPN 6,231,496, and make and use elongated magnetic nano-particles that have a tapered or sharp end as described by USPN 6,231,496 to enhance the shearing effect of cell disruption of the method WO 01/17611. Additionally, given that WO 01/17611 A1 teaches as using an alternating magnetic field up to 30 MhZ, the optimum suitable frequency ranges to rotate the nanoparticles may be obtained by routine experimentation, absent a showing of criticality or unexpected results. Furthermore, the addition of medication to the particles for treatment and injection of the particles would have been obvious as the coating particles with medicine for treatment and

injection of therapeutic agents are routine method is the art for medical treatment as shown by USPN 6,231,496.

8. All other objections and rejections recited in of June 5, 2009 are withdrawn.

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Peter J Reddig/

Examiner, Art Unit 1642